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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/428,692	10/28/1999	DANIEL B. CARR	2004117-0002	4992

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EXAMINER
LANDSMAN, ROBERT S

ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/428,692	Applicant(s) CARR ET AL.	
	Examiner Robert Landsman	Art Unit 1647	

-- The MAILING DATE of this communication appears on the c ver sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,28-33,45-52,54,55,57-59,61-64,69-74,86-93,95,96,98-100 and 102* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Formal Matters

A. Claims 1,2 and 24-102 were pending and claims 1, 2, 24-33, 45-52, 54, 55, 57, 60-74, 86-93, 95, 96, 98, 101 and 102 were the subject of this Office Action. In Amendment C, filed 10/11/02, Applicants cancelled claims 24-27, 34-44, 60, 65-68, 75-85 and 101. In view of the response to the Election by Original Presentation below, the Examiner has combined claims 58, 59, 99 and 100. Therefore, claims 1, 2, 28-33, 45-52, 54, 55, 57-59, 61-64, 69-74, 86-93, 95, 96, 98-100 and 102 are pending and are the subject of this Office Action.

B. All Statues under 35 USC not found in this Office Action can be found, cited in full, in a previous Office Action.

C. The Examiner appreciates Applicants' inclusion of a clean set of the pending claims.

2. Election by Original Presentation

A. Claims 58, 59, 99 and 100 were originally restricted from the claims reciting only SEQ ID NO:3 and 21 since these sequences are all independent. Applicants have argued that SEQ ID NO:42 and 43 are chimeras of SEQ ID NO:3 and 21. In view of this, the Examiner has recombined claims 58, 59, 99 and 100 with the elected Group.

3. Claim Objections

A. The Examiner appreciates Applicants' including claims 34-44 and 75-85 in their discussion of chimeric peptides, which the Examiner omitted. Applicants have canceled these claims. Applicants argue that, upon the allowance of a generic claim, Applicants should be entitled to consideration of claims to additional MOR binding species (SEQ ID NO:1, 2 and 4-11) and SP binding moieties (SEQ ID NO:25-30, 36 and 38-41). These arguments have been considered, but are not deemed persuasive. Though each of the additional 21 SEQ ID NOs may be considered species of the generic claim, they are still independent and distinct and would require different searches. However, if generic claims are found allowable, the Examiner will *consider* including one or more additional SEQ ID NOs.

B. All remaining claim objections have been withdrawn in view of Applicants' amendments, or cancellation of the claims which have been objected to.

4. Claim Rejections - 35 USC § 112, first paragraph – scope of enablement

A. Claims 31-33, 45, 49, 53, 56, 57, 72-74, 86, 90, 94, 97 and 98 remain rejected under 35 USC 112, first paragraph, for the reasons already of record on pages 4-7 of the Office Action dated 6/6/2 and claims 1, 2, 28, 29-33, 45-57, 61-64, 86-98 and 102 are newly rejected under 35 USC 112, first paragraph. Claims 31-33, 45, 49, 53, 56, 57, 72-74, 86, 90, 94, 97 and 98 remain rejected since they recite "**derivatives**." Claims 1, 2, 28, 29-33, 45-57, 61-64, 86-98 and 102 are rejected because the specification, while being enabling for the claimed chimeras wherein the mu opioid receptor binding moiety is an "**agonist**," does not reasonably provide enablement for chimeras in which the mu opioid receptor binding moiety is other than an agonist (i.e. antagonist or inverse agonist). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The Examiner agrees that Applicants are enabled for mu opioid receptor peptide agonists other than those listed in Table I of the specification and for SP peptide agonists other than those in Table 4, as well as for pharmaceutical compositions using these chimeras. However, regarding "derivatives," the specification discloses that these comprise molecules which can either hybridize to, or recognize an epitope of some polynucleotide or protein, respectively. It is believed that the molecules to which these derivatives will hybridize are those encoding mu opioid agonist, or SP agonist peptides, or that they will bind an antibody which specifically binds these agonists. However, this definition is not clear. Furthermore, the specification discloses that these molecules can be as little as 30% homologous to opioid or SP agonist moieties. However, respectfully, not only is it not clear what the "reference" compounds are (e.g. known opioid/SP agonists), but no specific hybridization conditions have been recited in the claims or specification, only the citation of a reference which teaches exemplary conditions. Therefore, any moietiy which is at least 4 amino acids in length would be covered by the claims, regardless of its structure or the number of substitutions, whether or not these agonists were known at the time of the invention. Applicants argue that derivatives are further defined on page 11, lines 13-23. However, these limitations only exemplify certain types of molecules, namely those which are based largely (i.e. "substantially the same") on known moieties. Applicants have not identified which residues would be required in order to maintain "functional equivalents" of these wild-type molecules.

In addition, Applicants have argued that they have enabled screening methods to identify opioid antagonists to be used in the chimeras of the invention (page 12 of the Response dated 10/11/02). However, the basis for Applicants' invention is that opioid agonists coupled to SP agonists are, unexpectedly, analgesic. Applicants have provided no guidance or working examples of chimeras

comprising opioid binding moieties other than peptide agonists that can be used to produce analgesia, nor is it predictable to one of ordinary skill in the art that opioid ligands other than peptide agonists would, when coupled to SP agonists, produce analgesia. Applicants have not enabled this excessive breadth.

Therefore, in summary, due to the lack of guidance and working examples of opioid and SP agonist derivatives, or opioid moieties other than agonists, as well as the lack of predictability as to which derivatives would possess this analgesic property, or as to which compounds other than opioid agonists would have the desired characteristics, the Examiner has concluded that undue experimentation would be required to practice the claimed invention.

5. Claim Rejections - 35 USC § 112, first paragraph – written description

A. Claims 31-33, 45, 49, 53, 56, 57, 72-74, 86, 90, 94, 97 and 98 remain rejected under 35 USC 112, first paragraph, for the reasons already of record on pages 8-9 of the Office Action dated 6/6/2 and claims 1, 2, 28, 29-33, 45-57, 61-64, 86-98 and 102 are newly rejected under 35 USC 112, first paragraph. Claims 31-33, 45, 49, 53, 56, 57, 72-74, 86, 90, 94, 97 and 98 remain rejected since they recite "**derivatives**." Claims 1, 2, 28, 29-33, 45-57, 61-64, 86-98 and 102C are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants' arguments for this rejection are substantially the same as for the rejection under 35 USC 112, first paragraph, above regarding scope of enablement and the same arguments by the Examiner are applicable here. However, Applicants have provided no written description for opioid moieties other than agonists which can be combined with SP moieties to produce a chimera. The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claims do not provide any guidance as to what changes should be made to produce compounds other than mu agonists which can couple to SP agonists to produce analgesia. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, "mu opioid peptide binding moieties" alone is insufficient to describe the genus. One of skill in the art would reasonable conclude that the disclosure fails to provide a

representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus at the time the invention was made.

6. Claim Rejections - 35 USC § 112, second paragraph

A. All rejections under 35 USC 112, second paragraph, have been withdrawn in view of Applicants' cancellation, arguments, or amendments to the claims.

7. Claim Rejections - 35 USC § 103

A. All rejections under 35 USC 103 have been withdrawn in view of Applicants' arguments that the References used in these rejections do not anticipate, or make obvious, the present invention.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
March 13, 2003